Complete Summary

GUIDELINE TITLE

Staging evaluation for patients with Hodgkin's disease.

BIBLIOGRAPHIC SOURCE(S)

Wolkov HB, Constine LS, Yahalom J, Chauvenet AM, Hoppe RT, Abrams RA, Deming RL, Mendenhall NP, Morris DE, Ng A, Hudson MM, Winter JN, Mauch PM. Staging evaluation for patients with Hodgkin's Disease. [online publication]. Reston (VA): American College of Radiology (ACR); 2005. 15 p. [61 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Wolkov HB, Elman AJ, Hoppe RT, Pistenmaa DA, Mauch PM, Constine LS, Deming RL, Dosoretz DE, Prosnitz LR, Yahalom J, Chauvenet A, Connors JM, Glick JH, Leibel S. Staging evaluation for patients with Hodgkin's disease. American College of Radiology. ACR Appropriateness Criteria. Radiology 2000 Jun; 215 (Suppl): 1207-23.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

COMPLETE SUMMARY CONTENT

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis RECOMMENDATIONS

EVIDENCE SUPPORTING THE RECOMMENDATIONS

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS QUALIFYING STATEMENTS

IMPLEMENTATION OF THE GUIDELINE

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Hodgkin's disease

GUIDELINE CATEGORY

Evaluation

CLINICAL SPECIALTY

Oncology Radiology

INTENDED USERS

Health Plans Hospitals Managed Care Organizations Physicians Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of radiologic procedures for the evaluation of Hodgkin's disease

TARGET POPULATION

Patients with Hodgkin's disease

INTERVENTIONS AND PRACTICES CONSIDERED

- 1. Computed tomography
 - Chest
 - Abdomen
 - Pelvis
 - Neck
- 2. Nuclear medicine
 - Positron emission tomography scan
 - Gallium scan
 - Bone scan
- 3. Magnetic resonance imaging
 - Chest
 - Abdomen
- 4. Laboratory tests
 - Complete blood count with differential
 - Liver function study
 - Erythrocyte sedimentation rate
 - Serum albumin
 - Beta 2 microglobulin
 - Soluble CD30
- 5. Bone marrow biopsy
- 6. Chest radiograph

MAJOR OUTCOMES CONSIDERED

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Flectronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of recent peer-reviewed medical journals, and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

The total number of source documents identified as the result of the literature search is not known.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed for reaching agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi

technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed by participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1-9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by the Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Clinical Condition: Staging Evaluation for Patients with Hodgkin's Disease

<u>Variant 1</u>: Child with biopsy-proven CS IIA NSHD presenting with neck nodes and mediastinal disease on chest radiograph.

| Radiologic Exam Procedure | Appropriateness Rating | Comments | |
|---|---------------------------|---|--|
| Computed Tomography | | | |
| Chest | 9 | | |
| Abdomen | 9 | | |
| Pelvis | 9 | | |
| | Nuclear M | edicine | |
| PET scan | 8 | | |
| Gallium scan | 4 | Only if PET not available | |
| Bone scan | 2 | | |
| Magnetic Resonance I maging | | | |
| Chest | 2 | | |
| Abdomen | 2 | | |
| Laboratory Tests | | | |
| CBC with differential | 9 | | |
| Liver function study | 9 | | |
| Erythrocyte sedimentation rate | 8 | | |
| Serum albumin | 8 | | |
| Beta 2 microglobulin | 2 | | |
| Soluble CD30 | 2 | | |
| Bone marrow biopsy | 4 | Indicated if platelet, WBC, or RBC counts are below normal. | |
| Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate | | | |

<u>Variant 2</u>: Young adult, male, with biopsy-proven CS IIIB NSHD with bulky mediastinal disease on chest radiograph and three para-aortic nodes on abdominal pelvic CT scan, located between L2-L4, measuring 1-1.5 cm.

| Radiologic Exam Procedure | Appropriateness Rating | Comments | | |
|---|---------------------------|---------------------------|--|--|
| Chest CT | 9 | | | |
| Bone marrow biopsy | 9 | | | |
| | Nuclear M | edicine | | |
| PET scan | 8 | | | |
| Gallium scan | 4 | Only if PET not available | | |
| Bone scan | 2 | | | |
| | Magnetic Reson | ance I maging | | |
| Chest | 2 | | | |
| Abdomen | 2 | | | |
| | Laboratory Tests | | | |
| CBC with differential | 9 | | | |
| Liver function study | 9 | | | |
| Erythrocyte sedimentation rate | 8 | | | |
| Serum albumin | 8 | | | |
| Soluble CD30 | 4 | | | |
| Beta 2 microglobulin | 2 | | | |
| Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate | | | | |

<u>Variant 3</u>: Young adult, male, with bulky mediastinal disease on chest radiograph, biopsy-proven CS 1A NSHD.

| Radiologic Exam Procedure | Appropriateness Rating | Comments |
|------------------------------|---------------------------|----------|
| Computed Tomography | | |
| Chest | 9 | |

| Radiologic Exam Procedure | Appropriateness Rating | Comments | |
|---|---------------------------|---|--|
| Abdomen | 9 | | |
| Pelvis | 9 | | |
| | Nuclear M | edicine | |
| PET scan | 8 | | |
| Gallium scan | 4 | Only if PET not available | |
| Bone scan | 2 | | |
| Magnetic Resonance I maging | | | |
| Chest | 2 | | |
| Abdomen | 2 | | |
| | Laboratory Tests | | |
| CBC with differential | 9 | | |
| Liver function study | 8 | | |
| Erythrocyte sedimentation rate | 8 | | |
| Serum albumin | 8 | | |
| Beta 2 microglobulin | 2 | | |
| Soluble CD30 | 2 | | |
| Bone marrow biopsy | 2 | Indicated if platelet, WBC, or RBC counts are below normal. | |
| Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate | | | |

<u>Variant 4</u>: Young adult, male, with biopsy-proven CS 1A LPHD, high neck presentation.

| Radiolog | ic Exam | Appropriateness | |
|----------|---------|-----------------|----------|
| Proce | dure | Rating | Comments |

| Radiologic Exam Procedure | Appropriateness Rating | Comments | |
|---|---------------------------|---|--|
| Chest radiograph | 9 | Chest CT can be performed in lieu of chest radiograph. | |
| | Computed To | omography | |
| Neck | 9 | | |
| Chest | 9 | | |
| Abdomen | 9 | | |
| Pelvis | 9 | | |
| | Nuclear M | edicine | |
| PET scan | 8 | | |
| Gallium scan | 4 | Only if PET not available | |
| Bone scan | 2 | | |
| Magnetic Resonance I maging | | | |
| Chest | 2 | | |
| Abdomen | 2 | | |
| Laboratory Tests | | | |
| CBC with differential | 9 | | |
| Liver function study | 8 | | |
| Erythrocyte sedimentation rate | 8 | | |
| Serum albumin | 8 | | |
| Beta 2 microglobulin | 2 | | |
| Soluble CD30 | 2 | | |
| Bone marrow biopsy | 2 | Indicated if platelet, WBC, or RBC counts are below normal. | |
| Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate | | | |

<u>Variant 5</u>: Young adult, male, with biopsy-proven CS 1A NSHD, axillary presentation.

| Radiologic Exam Procedure | Appropriateness Rating | Comments | |
|---|---------------------------|---|--|
| Chest radiograph | 9 | Chest CT can be performed in lieu of chest radiograph. | |
| | Computed To | omography | |
| Chest | 9 | | |
| Abdomen | 9 | | |
| Pelvis | 9 | | |
| | Nuclear M | ledicine | |
| PET scan | 8 | | |
| Gallium scan | 4 | Only if PET not available | |
| Bone scan | 2 | | |
| Magnetic Resonance I maging | | | |
| Chest | 2 | | |
| Abdomen | 2 | | |
| Laboratory Tests | | | |
| CBC with differential | 9 | | |
| Liver function study | 8 | | |
| Erythrocyte sedimentation rate | 8 | | |
| Serum albumin | 8 | | |
| Beta 2 microglobulin | 2 | | |
| Soluble CD30 | 2 | | |
| Bone marrow biopsy | 2 | Indicated if platelet, WBC, or RBC counts are below normal. | |
| Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate | | | |

<u>Variant 6</u>: Elderly patient, any gender, with biopsy-proven CS IIIA MCHD, with a left supraclavicular node and single 2-cm retroperitoneal node at L2.

| Radiologic Exam Procedure | Appropriateness Rating | Comments |
|---|---------------------------|--|
| Chest radiograph | 9 | Chest CT can be performed in lieu of chest radiograph. |
| Bone marrow biopsy | 8 | |
| | Computed To | omography |
| Chest | 9 | |
| Abdomen | 9 | |
| Pelvis | 9 | |
| | Nuclear M | edicine |
| PET scan | 8 | |
| Gallium scan | 4 | Only if PET not available |
| Bone scan | 2 | |
| Magnetic Resonance I maging | | |
| Chest | 2 | |
| Abdomen | 2 | |
| Laboratory Tests | | |
| CBC with differential | 9 | |
| Liver function study | 9 | |
| Erythrocyte sedimentation rate | 8 | |
| Serum albumin | 8 | |
| Beta 2 microglobulin | 2 | |
| Soluble CD30 | 2 | |
| Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 | | |

| Radiologic Exam Procedure | Appropriateness Rating | Comments |
|--|---------------------------|----------|
| 1 = Least appropriate 9 = Most appropriate | | |

<u>Variant 7</u>: Young adult, male, with biopsy-proven CS IIA NSHD, presenting with infradiaphragmatic left inguinal and femoral nodes and a 2-cm left external iliac node on pelvic CT scan.

| Radiologic Exam Procedure | Appropriateness Rating | Comments | |
|--------------------------------|-----------------------------|---|--|
| Chest radiograph | 9 | Chest CT can be performed in lieu of chest radiograph | |
| | Computed To | omography | |
| Chest | 9 | | |
| Abdomen | 9 | | |
| | Nuclear M | ledicine | |
| PET scan | 8 | | |
| Gallium scan | 4 | Only if PET not available | |
| Bone scan | 2 | | |
| | Magnetic Resonance I maging | | |
| Chest | 2 | | |
| Abdomen | 2 | | |
| Laboratory Tests | | | |
| CBC with differential | 9 | | |
| Liver function study | 8 | | |
| Erythrocyte sedimentation rate | 8 | | |
| Serum albumin | 8 | | |
| Beta 2 microglobulin | 2 | | |
| Soluble CD30 | 2 | | |

| Radiologic Exam Procedure | Appropriateness Rating | Comments |
|---|---------------------------|---|
| Bone marrow biopsy | 2 | Indicated if platelet, WBC, or RBC counts are below normal. |
| Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate | | |

<u>Variant 8</u>: Child, female, with biopsy-proven CS IIA MCHD presenting with left supraclavicular adenopathy and a non-bulky mediastinal mass on chest radiograph.

| Radiologic Exam Procedure | Appropriateness Rating | Comments | |
|--------------------------------|-----------------------------|---------------------------|--|
| | Computed To | omography | |
| Chest | 9 | | |
| Abdomen | 9 | | |
| Pelvis | 9 | | |
| | Nuclear Medicine | | |
| PET scan | 8 | | |
| Gallium scan | 4 | Only if PET not available | |
| Bone scan | 2 | | |
| | Magnetic Resonance I maging | | |
| Chest | 2 | | |
| Abdomen | 2 | | |
| | Laborator | y Tests | |
| CBC with differential | 9 | | |
| Liver function study | 9 | | |
| Erythrocyte sedimentation rate | 8 | | |
| Serum albumin | 8 | | |

| Radiologic Exam Procedure | Appropriateness Rating | Comments | |
|---|---------------------------|---|--|
| Beta 2 microglobulin | 2 | | |
| Soluble CD30 | 2 | | |
| Bone marrow biopsy | 2 | Indicated if platelet, WBC, or RBC counts are below normal. | |
| Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate | | | |

<u>Variant 9</u>: Young adult, male, with initial supradiaphragmatic PS IIA NSHD has an apparent pelvic nodal relapse following subtotal lymphoid irradiation.

| Appropriateness Rating | Comments | | |
|-----------------------------|--|--|--|
| 9 | | | |
| 9 | Chest CT can be performed in lieu of chest radiograph | | |
| 8 | | | |
| Computed Tomography | | | |
| 9 | | | |
| 9 | | | |
| 9 | | | |
| Nuclear Medicine | | | |
| 8 | | | |
| 4 | Only if PET not available | | |
| 2 | | | |
| Magnetic Resonance I maging | | | |
| 2 | | | |
| 2 | | | |
| | Rating 9 9 8 Computed To 9 9 9 Nuclear M 8 4 2 Magnetic Resona | | |

| Radiologic Exam Procedure | Appropriateness Rating | Comments | |
|---|---------------------------|--------------------------------|--|
| Laboratory Tests | | | |
| CBC with differential | 9 | | |
| Liver function study | 9 | | |
| Erythrocyte sedimentation rate | 8 | | |
| Serum albumin | 2 | No data for relapsed patients. | |
| Beta 2 microglobulin | 2 | | |
| Soluble CD30 | 2 | | |
| Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate | | | |

<u>Variant 10</u>: Young adult, male, with initial PS IIIA NSHD treated with ABVD chemotherapy alone, now with an apparent neck recurrence.

| Radiologic Exam Procedure | Appropriateness Rating | Comments | |
|------------------------------|---------------------------|---|--|
| Repeat biopsy | 9 | | |
| Chest radiograph | 9 | Chest CT can be performed in lieu of chest radiograph | |
| Bone marrow biopsy | 8 | | |
| Computed Tomography | | | |
| Chest | 9 | | |
| Abdomen | 9 | | |
| Pelvis | 9 | | |
| Nuclear Medicine | | | |
| PET scan | 8 | | |
| Gallium scan | 4 | Only if PET not available | |

| Radiologic Exam Procedure | Appropriateness Rating | Comments | | |
|---|---------------------------|--------------------------------|--|--|
| Bone scan | 2 | | | |
| Magnetic Resonance I maging | | | | |
| Chest | 2 | | | |
| Abdomen | 2 | | | |
| Laboratory Tests | | | | |
| CBC with differential | 9 | | | |
| Liver function study | 9 | | | |
| Erythrocyte sedimentation rate | 8 | | | |
| Serum albumin | 2 | No data for relapsed patients. | | |
| Beta 2 microglobulin | 2 | | | |
| Soluble CD30 | 2 | | | |
| Appropriateness Criteria Scale 1 2 3 4 5 6 7 8 9 1 = Least appropriate 9 = Most appropriate | | | | |

In Hodgkin's disease, the purpose of staging is to define the anatomic extent of detectable disease. This provides prognostic information and can serve as the basis of rational treatment decisions.

The Ann Arbor staging system and subsequent proposed modifications include a designation based on clinical stage and pathological stage. Clinical stage is based on the results of the initial diagnostic biopsy, physical exam, laboratory data, and imaging studies. Pathological stage is based on the results of any additional biopsies, including bone marrow biopsy, percutaneous or laparoscopic biopsy of nodes, liver, and splenectomy.

Clinical Staging

History and Physical Examination

Clinical evaluation should include an initial history and physical examination to assess for signs and symptoms of Hodgkin's disease. Particular attention should be given to the presence of documented "B" symptoms since this represents an

important prognostic factor with therapeutic implications. A clinical history of bone pain or cardiovascular/pulmonary complaints may direct further evaluation.

Laboratory Studies

Baseline laboratory evaluation should include a complete blood count with a differential, liver function studies, and an erythrocyte sedimentation rate (ESR).

One study has demonstrated that patients who present with abnormal blood counts, elevated alkaline phosphatase or lactate dehydrogenase levels, or an elevated ESR are at higher risk for involvement of bone marrow. Another study has also demonstrated that an elevated ESR may be associated with a higher risk for abdominal involvement.

The International Prognostic Factors Project on Advanced Hodgkin's Disease identified a seven-factor prognostic scoring system that could predict five-year rates of freedom from progression of disease. The prognostic score, which also was predictive of overall survival, included a serum albumin level of less than 4 grams per deciliter, a hemoglobin level less than 10.5 grams per deciliter, male gender, age 45 years or older, stage IV disease, leukocytosis (white cell count of at least 15,000 per cubic millimeter), and a lymphocyte count of less than 600 per cubic millimeter or a count less than 8% of the white cell count, or both.

Other markers such as elevated serum copper, zinc, and soluble CD30 levels have been noted to correlate with disease activity but are currently not part of the standard evaluation of the patient with Hodgkin's disease.

Imaging Studies

Plain Chest Radiograph

Posterior-anterior (PA) and lateral chest radiographs are required in all patients because intrathoracic presentation of disease is common.

Mediastinal adenopathy can be quantified by several methods. One such method involves measuring the maximum width of the mediastinal mass divided by the maximal transverse thoracic diameter at the level of the diaphragm (i.e., mediastinal mass ratio) on a standing PA chest radiograph. A second method involves taking the ratio of the greater transverse tumor diameter to the internal thoracic diameter at the level of the T5-T6 interspace. Patients with large mediastinal adenopathy, which has been defined as either a mediastinal mass ratio greater than one-third, a mass greater than 35% of the thoracic diameter at T5-T6, or a mass measuring more than 5-10 cm in width, are at increased risk for relapse when treated with radiation therapy alone.

Computed Tomography

Contrast-enhanced CT should be performed of the chest, abdomen, and pelvis in all patients.

Thoracic CT scans can result in upstaging of the patient by demonstrating abnormalities not appreciated on routine chest radiographs. Demonstration of intrathoracic abnormalities may also result in alteration of treatment fields or clinical management. Adenopathy in the mediastinal, hilar, subcarinal, and internal mammary areas may be detected with a thoracic CT scan, which can influence radiation treatment planning. Detection of extensive pericardial involvement or pulmonary parenchymal involvement can occasionally be demonstrated on chest CT scans and may alter the treatment plan.

CT scans of the abdomen have the ability to assess the upper abdominal nodes, the liver, and the spleen.

A CT of the neck may be helpful, especially in the situation where limited radiation therapy (involved field) is planned and the precise localization of enlarged lymph nodes in the neck will affect design of the radiation fields.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) may be an alternative to chest or abdominal CT scanning for initial evaluation of the patient.

MRI has been evaluated as an initial staging tool compared with CT scan in a prospective study. Employing laparotomy to define pathologic extent of abdominal disease, investigators demonstrated that MRI was more sensitive but less specific than CT with similar accuracy rates.

Another study investigated the role of MRI in the initial staging of Hodgkin's disease and found this procedure to be a useful adjunct for staging thoracic disease and assessing the spleen. MRI has been used in evaluating the bone marrow to identify areas of abnormality for biopsy. Due to its low sensitivity (55.6%) and its low positive predictive value (38.5%), it is not a substitute for bone marrow biopsy in appropriate patients.

Some investigators have found MRI to be of benefit in restaging patients following definitive treatment to help differentiate fibrosis from tumor.

Nuclear Medicine Studies

Several imaging agents have been investigated in staging Hodgkin's disease, including gallium-67, fluorodeoxyglucose (FDG), technetium 99m, somatostatin, and thallium. They are utilized in the initial staging of Hodgkin's disease and in patients at risk for relapse who have residual radiographic abnormalities during or after completion of therapy.

Investigators looking at the role of gallium in the initial staging of Hodgkin's disease have observed a sensitivity of 64-80% and a specificity of 96%-98%. One study compared gallium scans to CT evaluation, physical exam, and lymphangiography. The authors concluded that initial staging with gallium scans was of no benefit in the majority of patients with Hodgkin's disease. Another study demonstrated a negative predictive value of 28% in a series of patients who were staged with laparotomy. Other investigators noted a low sensitivity of gallium

scans in evaluating initial disease sites but found them to be of value in distinguishing fibrosis from Hodgkin's disease following treatment in the setting of residual radiographic abnormalities.

PET imaging has been used in the initial staging of Hodgkin's disease. One study reported on the pretreatment evaluation of 44 newly diagnosed patients with Hodgkin's disease using FDG-PET scans. As a consequence of PET imaging, five patients were upstaged and one patient was downstaged. PET scans were reported false positive in two patients and failed to visualize Hodgkin's disease in four patients. Another study retrospectively analyzed 44 patients staged with PET imaging and CT scans. One hundred and fifty nine sites of disease were demonstrated on PET imaging compared to 84 sites on CT. Eighteen patients (40.9%) were upstaged, nine with extranodal or splenic sites not identified on CT imaging.

Several studies have suggested that PET imaging is superior to gallium imaging in staging of Hodgkin's disease. One of these studies reported FDG-PET had a superior ability to clinically detect splenic disease compared with gallium imaging. PET scans demonstrated suspected disease below the diaphragm in three of five patients having FDG uptake in isolated splenic nodules that were not detected by gallium imaging. Another study compared PET imaging with conventional imaging methods in staging patients with Hodgkin's disease. The investigators reported an accuracy rate of 96% for PET versus 56% for conventional imaging.

Post treatment nuclear scintigraphy may help predict clinical outcome. Several authors have noted a significant difference in survival or an increased risk or relapse in patients who have a positive post treatment restaging gallium study. However, conversion of an initially positive study to a negative study following treatment does not rule out a subsequent relapse, particularly in the setting of stage III or IV disease.

Several investigators have demonstrated a potential role for PET imaging in conjunction with CT evaluation in the assessment of patients with residual masses following treatment. One study evaluated post treatment residual masses with PET imaging in patients with Hodgkin's disease and non-Hodgkin's lymphoma. Of 43 patients with Hodgkin's disease, no recurrences were noted in 39 patients with a negative PET scan; however, one of four patients with a positive scan relapsed. Another study compared PET to conventional CT imaging in the post treatment setting in patients with lymphoma (19 patients with Hodgkin's disease). They reported an increased relapse rate in patients with a positive post-treatment PET scan. Other investigators have recently reported similar results.

Pathological Staging

Bone Marrow Biopsy

In retrospective studies, the incidence of bone marrow involvement is low, approaching 5%. Bone marrow biopsy should be performed on patients with an abnormal complete blood count, "B" symptoms, advanced clinical stage, elevated alkaline phosphatase, or symptoms of bone pain.

Results from the German Hodgkin's Lymphoma Study Group demonstrate that the probability of bone marrow involvement increases with evidence of subdiaphragmatic disease (massive splenic involvement), more than one site of lymphatic involvement, the presence of "B" symptoms, and advanced clinical stage before bone marrow biopsy. Independent parameters when predicted for bone marrow involvement based on a logistic regression analysis included "B" symptoms (p<.00005); thrombocytopenia (p<.00005); large mediastinal tumor (p<.00005); stage before bone marrow biopsy (p=.00014); lactate dehydrogenase (LDH) level (p=.0004); and hemoglobin level (p=.0088).

Restaging

Following treatment for bulky mediastinal presentation of Hodgkin's disease, approximately 60% of patients will demonstrate residual adenopathy on a chest radiograph.

To avoid invasive restaging procedures, gallium scans and MRI have been used to ascertain whether a residual abnormality on chest radiograph represents fibrosis or viable tumor, with mixed results. Most investigators have found some predictive value; however, a significant number of false-negative and false-positive results have rendered these tests far from ideal. PET imaging may be more sensitive than gallium imaging in the restaging of patients with Hodgkin's disease. A negative result of these studies should not change further follow-up because subsequent relapse can occur. However, a positive result may suggest the need for additional tests, including biopsy if the implication of treatment failure is institution of additional therapy. Immunoscintigraphy and biological markers have also been used in an experimental setting to assess the question of persistent disease.

Conclusion

Staging procedures will continue to evolve as we develop new technological advances and our understanding of this disease process increases. New therapeutic approaches to this disease may also impact on our diagnostic evaluation of the patient.

Abbreviations

- ABVD, chemotherapy consisting of doxorubicin, bleomycin, vinblastine, and dacarbazine
- CBC, complete blood count
- CS, clinical stage
- CT, computed tomography
- LPHD, lymphocyte predominant Hodgkin's disease
- MCHD, mixed cellularity Hodgkin's disease
- NSHD, nodular sclerosis Hodgkin's disease
- PET, positron emission tomography
- PS, pathologic stage
- RBC, red blood cell
- WBC, white blood cell

CLINICAL ALGORITHM(S)

Algorithms were not developed from criteria guidelines.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVI DENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Selection of appropriate radiologic imaging procedures for the evaluation of patients with Hodgkin's disease

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

An American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to quide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about <u>availability</u>, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Wolkov HB, Constine LS, Yahalom J, Chauvenet AM, Hoppe RT, Abrams RA, Deming RL, Mendenhall NP, Morris DE, Ng A, Hudson MM, Winter JN, Mauch PM. Staging evaluation for patients with Hodgkin's Disease. [online publication]. Reston (VA): American College of Radiology (ACR); 2005. 15 p. [61 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 (revised 2005)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

GUI DELI NE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel on Radiation Oncology--Hodgkin's Disease Work Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Harvey B. Wolkov, MD (Principal Author); Louis S. Constine, MD (Co-author); Joachim Yahalom, MD (Co-author); Allen M. Chauvenet, MD (Co-author); Richard T. Hoppe, MD (Hodgkin's Work Group Panel Chair); Ross A. Abrams, MD; Richard L. Deming, MD; Nancy P. Mendenhall, MD; David Eric Morris, MD; Andrea Ng, MD; Melissa M. Hudson, MD; Jane N. Winter, MD; Peter M. Mauch, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Wolkov HB, Elman AJ, Hoppe RT, Pistenmaa DA, Mauch PM, Constine LS, Deming RL, Dosoretz DE, Prosnitz LR, Yahalom J, Chauvenet A, Connors JM, Glick JH, Leibel S. Staging evaluation for patients with Hodgkin's disease. American College of Radiology. ACR Appropriateness Criteria. Radiology 2000 Jun; 215 (Suppl): 1207-23.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the <u>American College of Radiology (ACR) Web site</u>.

ACR Appropriateness Criteria® Anytime, Anywhere $^{\text{TM}}$ (PDA application). Available from the ACR Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

 ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the <u>American College of Radiology (ACR) Web site</u>.

PATIENT RESOURCES

None available

NGC STATUS

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